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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,403	06/20/2005	Jose Manuel Francisco Lara Ochoa	2099.0090000/VLC/UWJ	3497

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EXAMINER	
RAE, CHARLESWORTH E	
ART UNIT	PAPER NUMBER
1611	
MAIL DATE	DELIVERY MODE
07/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,403	OCHOA, JOSE MANUEL FRANCISCO LARA	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-9 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-9, and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement is made of applicants' filing of the instant application as a Request for Continued Examination (RCE) under 37 CFR 1.1114, received 2/14/08.

Status of the Claims

Claims 1, 3, 4, 5, 6, 7, 8, 9, and 11 are currently pending in this application and are the subject of the Office action.

Claim 8 has been amended to recite the term "in a solid dosage form."

Response to applicant's arguments/remarks

Rejection under 102(b) (see applicant's Response at pages 4-5) = claims 8,9, and 11

Applicant contends that this rejection should be withdrawn for essentially the following summarized reasons (see applicant's Response at pages 4-5):

1) Claim 8 is amended to recite "in a solid dosage form" which renders the rejection moot because the '957 patent does not disclose a solid formulation comprising metformin and glimepiride in the relative ratios recited in the instant claims (see MPEP 2131).

2) The '957 patent is directed to a liquid composition.

In response, the rejection is withdrawn in view of the amendment and applicant's persuasive arguments.

Rejection under 103(a

Applicant contends that this rejection should be withdrawn for essentially the following

summarized reasons (see applicant's Response at pages 5-11):

1) The cited prior art references do not support a prima facie case of obviousness.

2) The examiner has not provided evidence to show why a person of ordinary skill in the art would modify the teachings of the '957 to create the instant claimed solid formulation because an artisan would expect the combination to have an additive effect on blood glucose levels.

3) The '957 is silent regarding synergistic effect of the combination of a sulfonylurea and metformin. It is noted that a combination of metformin with glyburide at a ratio of 75:1 does not result in a synergistic lowering of blood glucose levels in a diabetic patient.

4) Applicant has unexpectedly discovered that the claimed solid formulation in a range of 500:1 to 500:2 of metformin/glimepiride exhibit a synergistic effect on reducing blood glucose levels in a diabetic patient. Yet, the examiner has failed to consider this factor.

5) The examiner has improperly used a 102 inherency argument in the context of a 103(a) rejection by arguing that to the extent that the weight ratios taugh by the prior art and the instant claims overlap, the synergistic effect of the composition is construed to be an inherent feature of the composition (see Office action, page 7).

In response, the rejection is maintained as applicant's arguments are not found to be persuasive to overcome the rejection for the reasons previously made of record in the Office action, mailed 11/14/07, at pages 5-8, and for the additional reasons:

a) It is the examiner's position that to the extent that the synergistic effect of the claimed combination of metformin/glimepiride falls withinin the range ratio of 500/1 to 500/2, which overlaps with the teaching of the cited reference, the composition taught by the cited reference impliedly teaches said a synergistic combination for lowering glood glucose levels.

b) The effect of lowering blood glucose level is an intended use limitation which does not confer patentability to the claimed composition.

For the above reasons, the rejection of record is deemed to be proper and is maintained.

REJECTIONS

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chandran et al. (US Patent 6,890,957 B2), in further view of Moeckel et al. (US Patent 5,955,106), and Ghebre-Sellassie et al.(US Patent 6,499,984).

Chandran et al. (US Patent 6,890,957 B2) teach liquid formulations for use in children and adults who are not able to swallow tablets (col. 2, lines 10-34). Chandran et al. also disclose that metformin and its salts, especially the hydrochloride are bitter and is usually marketed as a coated tablet wherein the coating is designed to mask any unpleasant taste (col. 2, lines 1-27). In particular, Chandran et al. teach a method of treating hyperglycemia comprising administering to a patient in need of treatment (including Type II diabetes) an antihyperglycemic effective amount of the liquid formulations, wherein the liquid formulations comprise metformin in an amount ranging from about 20 /ml to about 400 mg/ml (column 1, lines 46-53; column 3, lines 27-34; column 4, lines 4-18; column 9, lines 5-10; and column 15, lines 1-60). Instant claims 8, 9, and 11 are directed to *"[a] method for controlling blood glucose levels in a patient with type 2 diabetes."* Chandran et al. teach that the metformin or salt thereof may be in combination with one or more antihyperglycemic agents; the antihyperglycemic agent may be an oral antihyperglycemic agent e.g. a sulfonyl urea, such as glybyride, glimepride, glipizide, gluclazide, or chlorpropamide or other known sulfonyl ureas or other antihyperglycemic agents which act on the ATP-dependent channel of the B cells, wherein the metformin or salt are preferably employed in a weight ratio to the sulfonyl urea in the range from about 50:1 to about 300:1 (column 8, lines 1-17). The weight

ratio of metformin to glimepiride recited in the instant claims (ranging from 500/1 to 500/2) is found to overlap with the teaching of Chanran et al. (column 8, lines 1-17). The term *"synergistic combination of glimepiride and metformin or a pharmaceutically acceptable salt thereof"* is construed to be a coextensive characteristic of the composition "*wherein the weight ratio of glimepiride and metformin or a pharmaceutically acceptable thereof is about 1/500 to about 2/500."* Chandran et al. teach metforim hydrochloride (col. 2, lines 10-27); claims 9 and 11 recite the term "metformin hydrochloride." However, Chandran et al. do not teach a solid dosage form of metformin and glimepiride.

Moeckel et al. (US Patent 5,955,106) is added to show the general state of the art regarding solid dosage forms comprising metformin. Moeckel et al. teach improved methods for preparing metformin solid dosage forms, including tablets and capsules, comprising at least about 70% of metformin relative to the weight of the pharmaceutical composition, wherein the dosage form contain the highest possible content of metformin, and wherein the problem of capping associated with the granulation of metformin is solved (col. 1, line 27 to col. 9, line 56; see especially col. 1, line 27 to 5, line 46).

Ghebre-Sellassie et al.(US Patent 6,499,984) is added to show the general state of the art regarding the methods of preparing tablet dosage forms comprising antidiabetic drugs. Ghebre-Sellassie et al. teach methods of preparing tablet dosage forms of antidiabetic drugs, including glimepiride and metformin hydrochloride (see especially col. 9, lines 35-37).

Based on the improved method of preparing metformin taught by Moeckel et al., someone of skill in the art would have been motivated to combine the teachings of the above cited prior art to create the instant claimed inventive concept for use in type 2 diabetic patients who do not have problems swallowing tablets.

Thus, a person of ordinary skill in the art at the time the instant invention was made would have found it obvious to create the instant claimed invention with reasonable predictability.

Claim rejections – 35 USC 102 – Newly applied

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-9, and 11 are rejected under 35 USC 102(b) as being anticipated by Timmins et al. (US Patent 6,031,004).

Timmins et al. (US Patent 6,031,004) teach antihyperglycemic combinations of metformin and a sulfonylurea and methods of treatment using said combinations for treating hyperglycemia in patients with Type II diabetes, wherein glimepiride is disclosed as a preferred sulfonylurea antihyperglycemic agent for use in combination with mefformin, and wherein the metfomin/sulfonylurea are used in a ratio of 300/1 to about 50:1, preferably from about 250/1 to about 75:1 (col. 1, lines 7-12; col. 3, lines 28-45; col. 4, lines 16-27). Instant claimed invention is directed to a metformin-glimepiride

combination in a weight ratio of about 500/1 to about 250/1 (i.e. claims 1, and 3-7) and methods of treating hyperglycemia in Type II diabetes using said combinations (claims 8,9, and 11). The term “about 500/1 to about 250/1” as recited in claims 1 and 8 clearly overlaps with the teaching of Timmins et al. of a weight ratio of 300/1 to about 50:1 (col. 3, lines 39-45). The term “synergistic combination” as recited in claim 8 is construed to be an inherent feature of the composition wherein the metformin and glimepiride are present in a weight ratio of 500/1 to 500/2. Timmins et al. also disclose that metformin has a bitter taste and is usually market as a coated tablet (col. 1, lines 29-35). Applicant’s invention is directed to a solid dosage form, which is reasonably construed to encompass tablets. Instant claims 4-7 recite the term "at least one excipient" which is satisfied by the teaching of Timmins et al. of a pharmaceutically acceptable carrier (e.g. see reference claim 5). For the above reasons, claims 1, 3-9, and 11 are found to be anticipated by the cited reference.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

14 July 2008

/C. R./ Examiner, Art Unit 1611

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615